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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KUBELIK, ANNE R	
ART UNIT	**PAPER NUMBER**
1638	9

DATE MAILED: 10/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/818,921	LUNDQUIST ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on th cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 10-32* is/are pending in the application.

4a) Of the above claim(s) *1* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election without traverse of Group II (claims 10-32) in Paper No. 8 is acknowledged. Claims 1 and 10-32 are pending. Claim 1 is withdrawn from consideration as being drawn to a non-elected invention. Claims 10-32 are examined.

Specification

2. The title of the invention is not descriptive of the instant invention. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.

3. The abstract is not descriptive of the instant invention. A new abstract is required that is clearly indicative of the invention to which the claims are directed.

Information Disclosure Statement

4. The information disclosure statement filed 27 March, 2001, fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. Additionally, references for which the citation is not complete (*e.g.*, the author's name is missing) or that are not suitable documents for publishing on the face of the file (*e.g.*, search reports) have not been considered.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 10-24, 26-27 and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tomes et al (US 5,886,244, filed June, 1988) in view of each of Barton et al (1987, Plant Physiol. 85:1103-1109), Vaeck et al (1987, Nature 328:33-37) and Adang et al (1985, EP 142,924).

The claims are drawn to a method of transformation of maize by microprojectile bombardment with a nucleic acid encoding a *Bacillus thuringiensis* endotoxin, wherein the nucleic acid is "adjusted" to be more efficiently expressed in maize.

Tomes et al disclose a method of transformation of maize by microprojectile bombardment and regeneration into stably transformed plants (examples 1-4 and claims 1-11). Tomes et al used the selectable marker gene chloramphenicol acetyl transferase (column 6, lines 45-52) and the reporter gene beta glucuronidase (column 10, lines 50-56) expressed from the CaMV 35S promoter and the AdhI intron (Fig. 1-2 and column 10, lines 50-56), and suggest using marker genes that provide resistance to kanamycin, methotrexate and hygromycin (column 2, lines 21-22). The tissues used include embryogenic suspension cultures and immature embryos (column 6, lines 58-62, and column 4, lines 53-67). Because Tomes et al teach Mendelian inheritance of the gene transformed into the maize plants, (column 11, lines 58-61) they teach generation of progeny from the transformed plants and production of seed from the

progeny. Tomes et al do not disclose method of transformation of maize by microprojectile bombardment with a nucleic acid encoding a *Bacillus thuringiensis* endotoxin, wherein the nucleic acid is "adjusted" to be more efficiently expressed in maize.

Barton et al teach tobacco plants transformed with a vector encoding a truncated HD-1 Bt toxin expressed from the CaMV 35S promoter (pg 1105, right column, paragraph 2; Fig. 1; and pg 1106, left column, paragraph 3). The truncated HD-1 gene encodes about the N-terminal 50% of the endotoxin (pg 1105, right column, paragraph 2). The vector also has the selectable marker gene NPTII expressed from the Nos promoter (Fig. 1). Because the endotoxin gene is truncated, it would be more efficiently expressed in maize.

Vaeck et al teach tobacco plants transformed with a vector encoding a truncated Bt endotoxin or truncated Bt endotoxins fused in-frame to the neo or nptII gene (Figs. 1-2, and paragraph spanning pg 34-35).

Adang et al (1985) teach tobacco plants transformed with a vector encoding a truncated HD-73 Bt toxin expressed from the nos or phaseolin promoter (pg 37, paragraph 2; pg 45-51) the vector also has A gene conferring kanamycin resistance (paragraph spanning pg 41-42). Because the endotoxin gene is truncated (pg 39-41), it would be more efficiently expressed in maize.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of transformation of maize by microprojectile bombardment and regeneration into stably transformed plants taught by Tomes et al, to transform maize with the nucleic acids encoding the truncated HD-1 or HD-73 Bt endotoxins as described in each of Barton et al and Adang et al (1985) or fused in frame with a selectable marker or reporter gene, as described in Vaeck et al. One of ordinary skill in the art would have been motivated to do so because Adang et al (1985) suggest expressing the HD-73 gene in corn (pg 77), because a major

corn pest, corn earworm, is commonly used to test the effectiveness of Bt endotoxins (Barton et al, pg 1103, right column, paragraph 2) and because Barton et al suggest using the truncated Bt endotoxin expressed in plants to deter feeding by corn earworm (pg 1109, left column, paragraph 3). Tomes et al suggest expressing nucleic acids encoding proteins that impart insect resistance in plants (column 1, lines 28-32), and teach an effective method of maize transformation for accomplishing that. Substitution of a selectable marker gene that confers resistance to phosphinothricin for one that confers resistance to kanamycin, methotrexate or hygromycin is an obvious design choice.

7. Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tomes et al in view of each of Barton et al, Vaeck et al, and Adang et al (1985) as applied to claims 10-24, 26-27 and 29-32 above, and further in view of Adang et al (US 5,380,831, filed September, 1988).

The claims are drawn to a method of transformation of maize by microprojectile bombardment with a nucleic acid encoding a *B. thuringiensis* endotoxin, wherein the Bt endotoxin codons have been optimized for expression in maize.

The teachings of Tomes et al in view of each of Barton et al, Vaeck et al and Adang et al (1985) are discussed above. Tomes et al in view of each of Barton et al, Vaeck et al and Adang et al (1985) do not disclose Bt endotoxin genes in which the codons have been optimized for expression in maize.

Adang et al (1988) teach a method of codon optimization of Bt endotoxin genes, wherein the method is applied to optimization for expression in monocots like maize (examples 1-2 and claims 1-14). Adang et al exemplified the method using the Btt endotoxin gene.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of transformation of maize by microprojectile bombardment with

a nucleic acid encoding a *B. thuringiensis* endotoxin taught by Tomes et al in view of each of Barton et al and Adang et al (1985), to optimize the codons of the Bt endotoxin genes for expression in maize as described in Adang et al (1988). One of ordinary skill in the art would have been motivated to do so because Adang et al (1988) teach that endotoxin genes in which the codons are optimized for expression in the plant into which they are transformed are more highly expressed (column 3, lines 54-64; and column 9, lines 6-8) and by teaching maize codon usage patterns (column 11, lines 50-64), Adang et al imply that their method is intended to be use for expression of Bt endotoxins in maize.

8. Claims 10-15, 18-24, 27, 29 and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of Klein et al (1989, Plant Physiol. 91:440-444), Klein et al (1988a, proc. Natl. Acad. Sci. USA 85:4305-4309), Klein et al (1988b, Bio/technol. 6:559-563) and Sanford et al (US Patent 5,036,006, filed June, 1986) in view of Shillito et al (US Patent 5,350,689, filed November, 1988).

The claims are drawn to a method of transformation of maize by microprojectile bombardment with a nucleic acid encoding a *B. thuringiensis* endotoxin, wherein the nucleic acid is "adjusted" to be more efficiently expressed in maize.

Klein et al (1989) disclose a method of transformation of maize suspension cells by microprojectile bombardment (pg 440, right column, paragraph 2). Klein et al used the selectable marker gene NPTII and the reporter gene beta glucuronidase expressed from the CaMV 35S and Adh promoters and the AdhI intron (Fig. 1). Klein et al (1989) do not disclose maize cells regenerated into plants or transformed with a nucleic acid encoding a modified Bt endotoxin.

Klein et al (1988a) disclose a method of transformation by microprojectile bombardment of maize suspension cells derived from embryogenic callus (last paragraph of pg 4305, entire pg

4306). Klein et al used the selectable marker gene CAT expressed from the CaMV 35S and Adh promoters and the AdhI intron (Fig. 1). Klein et al (1988a) do not disclose maize cells regenerated into plants or transformed with a nucleic acid encoding a modified Bt endotoxin.

Klein et al (1988b) disclose a method of transformation by microprojectile bombardment of maize suspension cells derived from embryogenic callus (last paragraph of pg 562, entire pg 563). Klein et al (1988b) do not disclose maize cells regenerated into plants or transformed with a nucleic acid encoding a modified Bt endotoxin.

Sanford et al disclose a method of transformation of maize cells by microprojectile bombardment (claim 3). Sanford et al do not disclose maize cells regenerated into plants or transformed with a nucleic acid encoding a modified Bt endotoxin.

Shillito et al teach a method of regenerating fertile maize plants from callus or embryogenic suspension cells generated from immature embryos (column 13 to column 22, examples 10a-12e and claims 13-22). Shillito et al also disclose maize plants transformed with vectors comprising nucleic acids encoding *B. thuringiensis* endotoxins expressed from the CaMV 35 promoter (Examples 6a-6b). The vectors also comprise nucleic acids providing hygromycin or kanamycin resistance (Examples 7a-7e). Shillito et al also disclose vectors comprising nucleic acids encoding the N-terminal 50% of the *B. thuringiensis* endotoxins expressed from the CaMV 35 promoter (Examples 22-24); these vectors would more efficiently express the endotoxin in maize. Shillito et al teach production of progeny from the regenerated, transformed maize plants (column 21, lines 16-30).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of transformation of maize cells by microprojectile bombardment as taught by each of Klein et al (1989), Klein et al (1988) and Sanford et al, to regenerate the

cells into plants and to transform them with a nucleic acid encoding a modified Bt endotoxin as described in Shillito et al. One of ordinary skill in the art would have been motivated to do so because substitution of one transformation method with another is an obvious optimization of experimental parameters. Substitution of a selectable marker gene that confers resistance to phosphinothricin for one that confers resistance to kanamycin or hygromycin is an obvious design choice.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 10-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-33 of U.S. Patent No. 6,331,665.

The instant claims are drawn to a method of transformation of maize by microprojectile bombardment with a nucleic acid encoding a *B. thuringiensis* endotoxin, wherein the nucleic acid is "adjusted" to be more efficiently expressed in maize.

The claims of the issued patent are drawn to maize plants transformed with a nucleic acid encoding a Bt endotoxin, wherein the nucleic acid is adjusted to be more efficiently expressed in

maize. Dependent claims are drawn to maize plants transformed with a nucleic acid encoding Dh1 or HD73 endotoxin (claims 3 and 10-11), a truncated endotoxin (claims 5, 13 and 23-24), and the N-terminal 50% of the endotoxin (claim 25), and to use of vectors that also comprise a selectable marker that confers resistance to hygromycin, sethoxydim, haloxyfop, glyphosate, methotrexate, imidazoline, sulfonylurea, triazolopyromidine, s-triazine, bromoxynil, phosphinothricin, kanamycin, G418, 2,2-dichloropropionic acid or neomycin (claims 17-21), and uses any of the AdhIS or maize shrunken-2 first introns, or the CaMV 35S, 19S manopine synthase, nos, or octopine synthase promoters (claims 27-30). Dependent claims are drawn to mazie plants transformed with a Bt coding sequence fused in frame with an selectable marker coding sequence (claim 22) or where the vector also encodes a protease inhibitor (claim 26). The issued patent does not claim a method of producing those maize plants by microprojectile bombardment, but teaches the method in column 29, line 25, to column 30, line 50. The method taught by the issued patent includes use of callus derived form immature embryos (column 17, line 47, to column 18, line 16) and production of progeny and seed from the progeny (column 30, lines 34-51).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to produce the maize plants claimed in the issued patent by microprojectile bombardment as described the issued patent. One of ordinary skill in the art would have been motivated to do so because the instantly claimed method of maize transformation was used to produce the plants claimed in the issued patent.

11. Claims 10-15 and 18-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 5,484,956 in view of Adang et al (US 5,380,831, filed September, 1988).

The instant claims are drawn to a method of transformation of maize by microprojectile bombardment with a nucleic acid encoding a *B. thuringiensis* endotoxin, wherein the nucleic acid is "adjusted" to be more efficiently expressed in maize.

The claims of the issued patent are drawn to maize plants transformed with a nucleic acid encoding a Bt endotoxin, wherein the nucleic acid is introduced into the plant by microprojectile bombardment. The issued patent does not claim a method of transformation of maize by microprojectile bombardment with a nucleic acid encoding a *B. thuringiensis* endotoxin, wherein the nucleic acid is "adjusted" to be more efficiently expressed in maize. The issued patent does not claim a method of producing those maize plants by microprojectile bombardment, but teaches the method in column 24, line 44, to column 26, line 20. The method taught by the issued patent includes use of callus derived form immature embryos (column 15, lines 4-45) and production of progeny and seed from the progeny (column 20, lines 20-52 and column 24, lines 33-41), use of constructs conferring resistance to hygromycin (column 17, line 29, to column 18, line 49), and transformation with a Bt coding sequence fused in frame with an selectable marker coding sequence or a protease inhibitor expressed from the CaMV and nos promoters (column, lines 46-55)

The teachings of Adang et al are discussed above.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of maize transformation as taught by the issued patent, to adjust the *B. thuringiensis* endotoxin coding sequence to be more efficiently expressed in maize as described in Adang et al. One of ordinary skill in the art would have been motivated to do so because Adang et al (1988) teach that endotoxin genes in which the codons are optimized for expression in the plant into which they are transformed are more highly expressed (column 3,

lines 54-64; and column 9, lines 6-8) and by teaching maize codon usage patterns (column 11, lines 50-64), Adang et al imply that their method is intended to be use for expression of Bt endotoxins in maize.

12. Claim 28 is free of the prior art, given the failure of the prior art to teach or suggest a method of transformation of maize by microprojectile bombardment with a nucleic acid encoding a *B. thuringiensis* endotoxin, wherein the nucleic acid is "adjusted" to be more efficiently expressed in maize and wherein the vector also encodes a protease inhibitor.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Anne R. Kubelik, Ph.D.
October 8, 2002

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